REMARKS

Reconsideration of this Application is respectfully requested.

Status of the claims

Claims 1, 12, 13, 20, 41, 42, and 44 are amended herein. These changes introduce no new matter, and their entry is respectfully requested.

Claims 1, 3, 5-10, 12-14, 16-18, 20-27, 29, 31-37, and 39-44 are pending in the application. Claims 2, 4, 11, 15, 19, 28, 30, and 38 have been cancelled.

Based on the above amendments and the following remarks, applicant respectfully requests that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Claim Amendments

Applicants have amended independent claims 1, 12, 13, and 20 to more particularly claim the invention. Claims 41, 42, and 44 have been amended to correct inadvertent errors in wording in referring to the claims from which they depend. These amendments add no new matter, and their entry is respectfully requested.

Amended claim 1 now recites a method in which cells are added to a matrix and (in step b)) a lysis composition is added to a matrix. This amendment is fully supported by the specification, including paragraph [0089] and Examples 1, 2, 3 and 4. Paragraph numbering corresponds to that used in the corresponding published application, U.S. 2002/0012982 A1. Amended claim 12 is reworded to more clearly recite a method that further comprises adding to the matrix a composition that can disrupt membranes or inclusion bodies in order to elute proteins not solubilized by the first composition that is used to lyse, disrupt, or permeabilize the cells. Support for the amendment can be found, for example, in paragraph [0093] and in Example 5 and Example 6. Claim 13 has been amended to conform in language to amended claim 12, from which it depends. Claim 20 as amended recites a composition having chromatographic resins, filters or detection compositions as supported in the specification, for example, paragraph [0104].

Dependent claims 41, 42, and 44 have been amended to properly recite an apparatus.

Claim Rejections under 35 U.S.C. §102 (Condra)

The Examiner has rejected claims 1, 3, 7-9, 12, 13, 16, 17, 20-22, 24-27, 29, 31, and 32 as anticipated under 35 U.S.C. §102(b) by Condra (U.S. Patent No. 4,973,551). Applicants disagree that Condra anticipates these claims for at least the following reasons.

In the first case, Applicants note that the Office Action states on page 6, paragraph 3, "The primary reference of the '551 [Condra] patent differs from claims 1, 3, 5-10, 12-14, 16-18, 20-27, 29, 31-37 and 39-44 in not teaching the use of a pore-containing matrix with the pore sizes as claimed and a kit formulation thereof." In particular, independent claims 1 and 20 recite that the pores of the matrix have an average size ranging from about 0.1 micron to 1,000 microns in diameter, and independent claim 21 recites that the pores of the matrix have an average size ranging from about 0.1 micron to 10,000 microns in diameter. Because Condra does not disclose a matrix of the claimed pore sizes, Condra does not anticipate independent claims 1, 20, and 21, and claims 3, 7-9, 12, 13, 16, 17, 22, 24-27, 29, 31, and 32 dependent therefrom.

Applicants further disagree that Condra anticipates claims 1, 3, 7-9, 12, 13, 16, 17, 20-22, 24-27, 29, 31, and 32 for the following reasons. To more clearly state the invention, applicants have amended claim 1 to recite a method for isolating peptides or proteins that comprises contacting cells with a pore containing matrix, adding a lysis/disruption/permeabilization composition to the matrix in a separate step, and causing soluble peptide(s) or protein(s) to flow through the column. This is in contrast to Condra, in which a DE-52 column is used to isolate sporozoites from a preparation of "oocysts, sporocysts, and oocyst shells" (column 4, lines 67 to column 5, line 17). Condra does not include a step in which a lysis/disruption/permeabilization composition or compound is added to

the matrix "in an amount sufficient to lyse, disrupt, or permeabilize the cells" as recited in claim 1.

Condra discloses methods for isolating sporozoites of *E. tenella* and *E. acervulina* for identifying proteins for use in making poultry vaccines against these parasites. The use of pepsin by Condra is not for cell lysis as stated in the Office Action. Rather, pepsin is used in isolating (intact) oocysts from cecal (large intestinal) contents and feces of chickens. The oocysts (which are not cells, but cases oocytes that germinate to give rise ultimately to sporozoites) that are ultimately obtained from this isolation procedure are isolated intact. The DE-52 matrix cited by the Examiner is used by Condra to isolate intact sporozoites (the parasitic cells that divide in the gut of infected chickens). In the protocol set forth in Condra, oocysts of the parasites *E. tenella* and *E. acervulina* are isolated from chickens or chicken feces, purified, and allowed to sporulate (column 4, lines 30-49). Following sporulation, sporozoites (cells that "hatch" from the oocyst and divide in the host) are isolated from sporulated oocysts by grinding and treatment with trypsin and detergent to remove sporozoites from oocyst shells ("excysting"). At this point, the preparation is loaded on DE-52 anion exchange column to purify the sporozites which are not lysed, but intact.

After the isolation of intact sporocytes on the DE-52 column, "Purified sporozoites are disrupted by freezing and thawing at least 3 times, and sonicated until disrupted in PBS containing about 1 mM phenylmethysulfonylfluoride." (column 5 lines 17-20). Thus, not only is a lysis/disruption/permeabilization compound not added to the column, the sporocytes are not lysed by the addition of a compound at all, but rather are physically/mechanically disrupted.

The resulting "sporulated oocyst and sporozoite cell free preparations are separated by gel permeation chromatography,

preferably Sephadex S 200 (Pharmacia) in a separation buffer containing about 50 mM Na_2HPO_4-NaH_2PO_4, pH about 7.2 and about 0.1% Zwittergent 3-12." [emphasis added]. In this step, the mechanically disrupted preparation is loaded on the S 200 column. No lysis/disruption/permeabilization agent is used or added to the column. The detergent (Zwittergent 3-12) present in the solution that the preparation is suspended in is very mild and of very low concentration (0.1%) which would be inadequate for lysing cells, and is present to prevent aggregation in the column. (Applicants note that Example 1 repeats the protocol detailed in columns 4-5 of the specification as a specific example that does not differ in steps or detail from the quoted section.)

Thus, Condra also fails to disclose step b) of the method recited in claim 1: "adding to the at least one pore-containing matrix one or more lysis/disruption/permeabilization compositions or compounds in an amount sufficient to lyse, disrupt or permeabilize the cells;". Claim 1 therefore is not anticipated under 102(b) by Condra, and Applicants respectfully request that the rejection be removed.

Claims 3, 5-10, 12-14, and 16-18 are dependent on claim 1, and therefore incorporate all the elements of claim 1. As Condra does not disclose all the elements of claim 1, Condra also does not anticipate claims 3, 5-10, 12-14, and 16-18.

Claim 20 as amended herein recites a composition that comprises a lysis/disruption/permeabilization composition or compound, a pore-containing matrix, and at least one chromatographic resin that binds proteins or peptides, impurities, protein modifying reagents, enzymes, nucleic acids, an enzyme substrate, or filters, or compositions which detect or quantify the amount of protein or nucleic acid present in the sample. Applicants do not agree that Condra discloses the recited composition. As set forth above, Condra

does not disclose a lysis/disruption/permeabilization composition or compound in combination with a matrix. The sporozoites and oocysts used in Condra for identifying immunogenic proteins are disrupted mechanically, and not by means of a composition or compound. Further, Condra does not disclose a composition having a chromatographic resin that binds impurities, modifying reagents, proteins, peptides, substrates, or nucleic acids as recited, a filter, or a detection composition as set forth in amended claim 20. Applicants therefore contend that claim 20 is not anticipated by Condra.

Claim 21 is drawn to an apparatus that comprises a housing containing one or more pore-containing matrices that comprises one or more lysis/disruption/permeabilization compositions or compounds in an amount sufficient to lyse, disrupt, or permeabilize cells; and at least one chromatographic resin that binds proteins or peptides, impurities, protein modifying reagents, enzymes, nucleic acids, or an enzyme substrate, or filters, or compositions which detect or quantify the amount of protein or nucleic acid present in the sample. The Office Action does not provided any evidence that Condra discloses such a combination. Applicants contend that Condra does not disclose an apparatus that includes the recited elements. In the first case, Condra provides no teaching as to a housing having a matrix having pores of from 0.1 to 10,000 microns in diameter. As discussed above, Condra also does not include disclosure of a housing having a pore-containing matrix that comprises a chromatographic resin that binds proteins or peptides, impurities, protein modifying reagents, enzymes, nucleic acids, or an enzyme substrate, a filter, or a detection composition as set forth in claim 21. Thus, Condra does not disclose each and every element of claim 21, and therefore does not anticipate claim 21 or claims 22, 24-27, 29, 31, and 32 that depend from claim 21.

In not disclosing a matrix of the recited pore sizes, and in not disclosing a lysis/disruption/permeabilization buffer in combination with a matrix, Condra does not anticipate claims 1, 3, 7-9, 12, 13, 16, and 17. In not disclosing a matrix of the recited pore sizes, in not disclosing a lysis/disruption/permeabilization buffer in combination with a matrix, and in not disclosing a chromatographic resin, filter, or detection reagent as recited in claims 20 and 21, Condra does not anticipate claims, 20-22, 24-27, 29, 31, under 35 U.S.C. §102(b). Applicants therefore respectfully request that the rejection of these claims under §102(b)be removed.

Claim Rejections under 35 U.S.C. §103(a)

Condra, Shah, and Henco

Claims 1, 3, 5-10, 12-14, 16-18, 20-27, 29, 31-37, and 39-44 have been rejected as being obvious under 35 U.S.C. §103(a)over Condra (U.S. Patent No. 4,973,551) taken with Shah (U.S. Patent No. 4,303,530) and Henco (5,652,141).

Applicants disagree that the cited references render the claims obvious. To establish a prima facie case of obviousness, each and every element of the claims must be taught or suggested by the references. Applicants have already argued in the preceding section that Condra does not disclose all elements of claims 1, 3, 7-9, 12, 13, 16, 17, in that Condra does not disclose contacting a matrix with a) cells and b) a lysis/disruption/ permeabilization composition as pertain to claims 1, 3, 5-10, 12-14, and 16-18. As explained in that section, Applicants maintain that the "separation buffer" of Condra referred to in the Office Action does not constitute a lysis/disruption/ permeabilization composition or compound in an amount sufficient to lyse, disrupt or permeabilize the cells" as recited in independent claims 1, 20, and 21.

The Office Action has cited Shah providing disclosure of filters with pore sizes that overlap those recited in claims 1, 5, 6, 20, 21, and 41-44. However, Shah's filter is for isolating cells, not components of cells, and therefore motivation for combining this reference with Condra is lacking. Further, Shah does not make up for the lack of "a lysis/disruption/ permeabilization composition or compound in an amount sufficient to lyse, disrupt or permeabilize the cells", missing in Condra. Thus, Condra in combination with Shah does not render claims 1, 5, 6, 20, 21, and 41-44 obvious, and Applicants respectfully request that the rejection under 35 U.S.C. §103(a)be withdrawn.

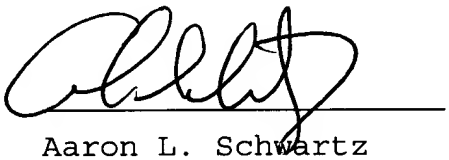
The Office Action has cited Henco in rejecting claims 21-27, 29, 31, and 32 drawn to an apparatus containing a housing, a pore-containing matrix, and a chromatographic resin. Applicants disagree, however, that Henco discloses an apparatus that comprises a pore-containing matrix that comprises one or more lysis/disruption/ permeabilization compositions or compounds in an amount sufficient to lyse, disrupt, or permeabilize cells. In Henco, a solution for lysing cells is not provided with the matrix, but is added separately to the apparatus (column 4, lines 66 and 67). Thus, Henco does not make up for the deficiencies of Condra. Claims 21-27, 29, 31, and 32 are not obvious under 35 U.S.C. §103(a), and Applicants respectfully request that the rejection be withdrawn.

Conclusion

All of the stated grounds of rejection have been properly traversed. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding rejections and that

they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.



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